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Effects of joint effusion on proprioception in patients with knee osteoarthritis: a single-blind, randomized controlled clinical trial

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SUMMARY

Objective: To assess the effects of joint effusion on proprioceptive status in patients with knee osteoarthritis (OA).
Design: A single-blind, randomized, controlled clinical trial in 40 female subjects aged 50 years and over with painful knee OA. All subjects were randomly assigned to either the control or experimental group. A volume of 20 mL of normal saline was injected into the knee joint cavity of subjects in the experimental group under ultrasonographic guidance. Proprioceptive acuity was assessed by active repositioning of the lower limb using an electrogoniometer to measure knee joint position sense (JPS) under both non-weight-bearing (NWB) and weight-bearing (WB) conditions twice, with a 20-min rest interval. The experimental group performed the task twice (Test 1 and Test 2) before and within 5 min after joint infusion. The control group also performed Test 1 and Test 2 without joint infusion. The outcome of interest was the absolute angular error (AAE), ignoring the direction of the error, between the randomized target angle and the patient's reproduced angle of JPS values.
Results: Compared with the control group, JPS was significantly compromised in the experimental group in the NWB test after joint infusion ($P = 0.025$). However, no significant differences in the angular error were observed between Test 1 and Test 2 in the control group for the NWB or WB test or in the experimental group for the WB test after infusion ($P > 0.05$).
Conclusions: This study showed that joint effusion impairs proprioceptive function in osteoarthritic knee joints.
Clinical trial number: NCT01060215 (ClinicalTrials.gov Identifier)

Introduction

Proprioception is a sensory modality that provides feedback on the internal status of the body and enables us to perceive joint position and motion. Awareness of the orientation of the body in space and the direction, extent, and rate of movement of the limbs is essential for limb position and coordinated movement. Although the roles of afferent and efferent signals in the judgment of limb position have been debated for over a century, the current consensus is that muscle spindles play a primary role in our sense of position and movement.[1] In addition, joint receptors, cutaneous receptors, and sense of effort also play roles in position sense, but their relative contributions have yet to be determined[1,2].

Osteoarthritis (OA), also called degenerative joint disease, is a major musculoskeletal condition characterized by loss of articular cartilage that leads to pain and loss of function.[3] The most commonly affected joint is the knee, and OA may result in changes that affect not only intracapsular tissues, but also periarticular tissues, such as ligaments, capsules, tendons, and muscles[4–6]. Many studies have examined the proprioceptive status of knee OA, and subjects with knee OA are known to have impaired proprioception compared with age-matched controls[7–9]. Elucidating the etiology of proprioceptive deficits in knee OA is important because proprioceptive acuity may be modifiable, and restoring proprioceptive function would allow the body to maintain stability and orientation during static and dynamic activities to prevent falls[10,11].

Joint effusion is a common symptom associated with a chronic degenerative joint condition[12]. Nevertheless, little is known about the effects of effusion on the knee joint as one of the various causes of

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proprioceptive deficits in knee OA. In patients with rheumatoid arthritis, altered proprioceptive sensations at finger joints were demonstrated compared to an age- and sex-matched control group[13]. Although disease process was different from OA, it suggested that these results may be due to the loss or distortion of afferent feedback from mechanoreceptors innervating the affected joint. A case study[14] revealed significant improvement of proprioceptive ability in the subject's passive repositioning sense following the aspiration of chronic effusion. This study provided an insight into the effects of effusion on the afferent feedback system of the capsular mechanoreceptors.

Jawed *et al.*[15] have previously shown that the resting intra-articular pressure (IAP) of OA patients with joint effusion is higher than that for acute traumatic knee effusion (ATE) without previous arthropathy. They also revealed that the rise of IAP during isometric quadriceps contraction in an OA group was significantly higher than that in an ATE group, and its magnitude was significantly correlated with the volume of synovial fluid aspiration in the OA group but not in the ATE group. We therefore postulated that the low compliance of the joint capsule in OA would also be a cause of the proprioceptive deficit in knee OA patients with joint effusion. Therefore, it is important to investigate whether the mechanical effect of effusion itself influences proprioception in the knee joint through the stimulation of capsular or intra-articular receptors. It should be noted that a previous study[16] has demonstrated that the injection of non-inflammatory fluid into the knee joint did not impair the joint proprioceptive ability in 20 subjects. However, this study was performed in healthy young subjects, and these data cannot be applied to OA patients.

We performed this trial to investigate whether the presence of fluid in the joint would impair proprioceptive acuity in symptomatic OA patients. The primary aim of this study was to assess proprioceptive acuity after joint infusion under non-weight-bearing (NWB) conditions and the secondary aim was to evaluate proprioceptive acuity after joint infusion under weight-bearing (WB) conditions.

Methods

Study design and subjects

The study was designed as a single-blind (blinded examiner), randomized parallel group, controlled clinical trial. Female subjects with knee OA were recruited from the Department of Rehabilitation Medicine at Seoul St. Mary's Hospital in South Korea. All subjects were 50 years old or over and had knee pain without joint effusion, which was confirmed by ultrasonography (US). They also fulfilled inclusion criterion (1) or at least two of criteria 2–6 established by the American College of Rheumatology (ACR)[17]: (1) Kellgren and Lawrence (K/L) grade $\geq$II; (2) morning stiffness $<$30 min in duration; (3) crepitus on movement of the knee joint; (4) bony tenderness at the knee joint margins; (5) palpable or visible bony enlargement; (6) no palpable warmth. Study exclusion criteria for all subjects were: (1) the presence of knee joint effusion determined by US; (2) a history of knee injury or surgery; (3) a history of knee injection within 3 months; (4) a history of inflammatory arthritis; (5) taking anticoagulants; (6) balance or gait disturbance; (7) diabetes mellitus.

Forty female subjects recruited to the study were randomly assigned to control or experimental groups following blocked randomization procedures; the block size was four. All subjects were sequentially allocated using computerized random numbers, and assignments were concealed from the subjects until the injection procedure. The random allocation sequence was generated by an investigator with no clinical involvement in the trial. One physiatrist enrolled participants, and another physiatrist assigned the subjects to either the control or experimental group. The proprioception examiner was blinded throughout the experiment. In cases of bilateral knee OA, the most symptomatic leg without fluid collection was tested. A volume of 20 mL of normal saline was injected into the knee joint cavity of the subjects in the experimental group under US guidance, and we confirmed the presence of fluid in the joint by US examination. US examination has been shown to be one of the best available non-invasive tools for the measurement of joint effusion[18–20]. Scheel *et al.*[18] demonstrated that US has an excellent inter-observer reliability (kappa value of 1) between 14 experts and a good sensitivity (91%) and specificity (88%) compared with magnetic resonance imaging (MRI) for diagnosing knee abnormalities. The subjects in the injection group were tested twice (Test 1 and Test 2) for joint position sense (JPS) before and after joint infusion with a 20-min interval, and the time from injection of fluid to Test 2 was approximately 5 min. The subjects in the control group were also tested twice with a 20-min rest interval, but without joint infusion.

All procedures for proprioceptive acuity measurement were performed by one examiner to maintain blinding for injection. WB anteroposterior and lateral radiographs of the knee in full extension were obtained, and the grading scales proposed by K/L were scored in a blinded manner by an experienced radiologist.

The study was approved by the Ethics Committee of the Catholic University of Korea and subjects' written consents were obtained from all subjects according to the Declaration of Helsinki.

Proprioception measurements

Proprioceptive acuity was assessed by active repositioning of the lower limb using an electrogoniometer to measure knee JPS under NWB and WB conditions.

To detect JPS, we used modifications of the methods widely used in other studies on knee proprioception, *i.e.*, passive-to-active and active-to-active angle reproduction in NWB and WB positions, respectively[9,14,21–25]. The knee joint angle was measured using an electronic dual inclinometer (Dualer IQ™; JTECH Medical, Salt Lake City, UT). In the starting position, this device was attached to the lateral aspect of the lower leg using double-sided medical tape, with the proximal electrogoniometer block just above the lateral femoral condyle in line with the greater trochanter, and the distal block just below the head of the fibula, aligned with the lateral malleolus. The blocks were connected to each other by an electric line, and the upper block gave a continuous, real-time digital reading of knee flexion angle.

In the starting position, the electrogoniometer display unit was zeroed before each test with the knee fully extended, yielding the actual knee flexion angle.

The subjects were blindfolded and tested in quiet surroundings to eliminate visual and auditory stimuli, and external auditory stimuli were limited to standardized commands by the examiner.

The subjects wore shorts with bare feet to eliminate any contribution of cutaneous receptors.

For each trial, proprioceptive acuity was taken as the difference between the knee angles at the target and reproduced positions. The outcome variable was the absolute angular error (AAE), which was the absolute difference, ignoring the direction of the error, between the randomized target angle and the patient's reproduced angle (*i.e.*, $|\mathrm{AAE} = \text{test angle}_{\text{reproduced}} - \text{test angle}_{\text{target}}|$).

Each subject performed three practice tests to become familiar with the test process before the actual test. A total of five randomized trials were completed, and the average was taken for the limb.

To avoid any learning effect, the order of target angles was randomly allocated for each subject using random drawings of papers written with the target angle. The order of two methods for JPS measurement was from the NWB to the WB test to avoid muscle fatigue.

Passive-to-active angle reproduction (NWB test)

Each subject was instructed to sit on the raised chair with the hips and knees at 90° flexion. From this start position with the legs dangling, the examiner passively extended one of the subject's lower legs to each of the target angles of 20°, 30°, 40°, 50°, and 60° of knee flexion in random order at an angular velocity of about 10°/s using an electronic metronome. The leg was held there for 5 s by the examiner to allow the subject to memorize the position. The subjects were instructed not to voluntarily contract their muscles to avoid afferent signals from muscle activity. Then, the examiner slowly returned the lower leg to the start position. After the 5-s interval, subjects were asked to actively reproduce the test angle with their eyes closed using the same leg. Patients acknowledged verbally when they believed that they had achieved the angle, and the knee angle displayed on the upper block at this reproduced position was recorded.

Active-to-active angle reproduction (WB test)

In the upright standing position, the subject was instructed to lift the unexamined foot from the floor and slowly flex the examined limb to each of the target angles of 20°, 25°, 30°, 35°, and 40° of knee flexion in random order, at an angular velocity of about 10°/s using an electronic metronome. The leg was held in this position for 5 s so that the subject could memorize the position, and the leg was then returned to the upright standing position. After the 5-s interval, the subject was asked to actively reproduce the previous unilateral WB position and to stop when she perceived the target angle of knee flexion had been reached. The examiner recorded the knee angle displayed on the upper block at this reproduced position. This test was performed with the subject standing barefoot on a firm, level surface using bilateral hand supports to prevent falling.

The holding times used here were the same as those in previous studies[9,23,24].

Statistical analyses

Statistical analysis was performed using SPSS, version 11.5. All tests were two-tailed, and $P < 0.05$ was taken to indicate statistical significance. The primary endpoint of this study was to assess proprioceptive acuity under NWB conditions and additional information was obtained under more functional situation, *i.e.*, the WB test as the secondary endpoint. Therefore, NWB and WB tests do not create multiplicity problems. Using data under the NWB condition[26], we calculated the sample size of 20 subjects per group, given an anticipated injection failure rate of 10% and a power of more than 80% to detect differences in the outcome. The Gaussian distribution was evaluated using the Shapiro–Wilk test. For normally distributed variables (height, body weight, body mass index (BMI), AAE differences between Test 1 and Test 2 for each group under both NWB and WB conditions, and AAE in the experimental group under NWB conditions), Student's *t*-test or the paired *t*-test was used. For non-normally distributed variables (age, AAE in the control group under both NWB and WB conditions, and AAE in the experimental group under WB conditions), the Mann–Whitney *U* test or Wilcoxon signed rank test was used. The K/L grade was compared between groups using the Fisher's exact test. The differences between Test 1 and Test 2 across the groups were assessed using ANCOVA with age, BMI, K–L grade, and baseline scores as covariates. These covariates were chosen because they might be associated with knee proprioceptive function. α equalled 0.826 and 0.829, and the intraclass correlation coefficients (ICCs), 95% confidence intervals (CI) for the tests of NWB and WB conditions were 0.70, [0.41, 0.86] and 0.72, [0.43, 0.87], respectively.

Results

Although 40 subjects were initially recruited from May 2009 to January 2010, one patient was unable to complete the study due to injection failure (Fig. 1). 10 left knees (10 right knees) in the control group and nine left knees (10 right knees) in the experimental group were assessed. The baseline characteristics of the 39 subjects that completed all procedures are given in Table I. No significant differences in age, height, body weight, BMI, or K/L grade were found between the two groups at baseline ($P > 0.05$) (Table I). And, there were no significant differences of AAE in Test 1 between the two groups ($P = 0.757$ in NWB test, $P = 0.272$ in WB test).

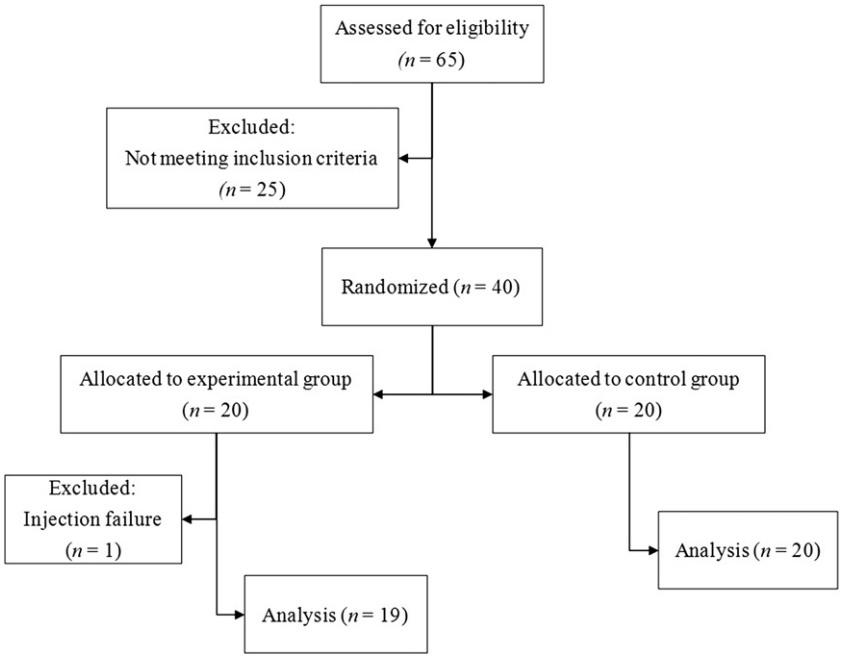

Fig. 1. Flow diagram of patients' progress through the design of the study.

Table I
Baseline characteristics in the control and experimental groups*

	Control group ($n=20$)	Experimental group ($n=19$)	P-value†
Age, years	57.8 ± 5.3	59.6 ± 4.5	0.176
Height, cm	157.2 ± 4.0	156.1 ± 5.4	0.495
Body weight, kg	59.7 ± 6.8	57.7 ± 7.2	0.388
BMI, kg/m^2	24.1 ± 2.3	23.7 ± 2.7	0.576
K/L grade, number			0.793
I	1	0	
II	10	9	
III	6	9	
IV	3	1	

* Values are the means ± SD unless indicated otherwise.
† Comparison between control and experimental groups.

The adjusted mean differences between two groups were 1.41, 95% CI [0.18, 2.63] for the NWB test and 0.47, 95% CI [−0.28, 1.23] for the WB test. Compared with the control group, JPS was significantly poorer in the experimental group in the NWB test after joint infusion ($P=0.025$). However, no significant changes in the angular error between Test 1 and Test 2 were found in the control group for the NWB or WB test or in the experimental group for the WB test after infusion ($P>0.05$) [Table II, Fig. 2(A and B)].

Discussion

To our knowledge, this is the first randomized, controlled clinical trial to evaluate the effects of joint effusion on proprioception using an experimental model of degenerative OA. The results of this study indicated that knee JPS in the NWB test was impaired after joint infusion in the symptomatic knees of OA patients. These observations suggest that the presence of fluid in the joint may contribute to the proprioceptive deficits in knee OA.

Proprioceptive acuity declines with age, and it declines more in arthritic knees of OA subjects than in those of age- and sex-matched control subjects[7–9,27–29]. Although it is unclear whether proprioceptive deficits in knee OA may contribute to and/or result from knee OA, many studies have indicated that proprioceptive deficit is a risk factor in progression and poor functional outcome of knee OA[22,30–32]. In a recent large longitudinal study[22], those with the worst proprioceptive acuity under NWB conditions at baseline had slightly greater worsening of pain and physical function scores compared with those with the best proprioceptive acuity.

A previous study[16] indicating that non-inflammatory fluid injection into the healthy knee joint did not impair joint proprioceptive ability suggested that the effects of long-term effusion and the nature of the inflammatory fluid may be more responsible for the loss of proprioception. The current study investigated the mechanical effects of acute effusion in OA patients and revealed that the acute infusion of non-inflammatory fluid could impair proprioception in the degenerative knee joint.

Various explanations can be offered for a decline in proprioceptive acuity after joint infusion under NWB conditions. First, the presence of fluid could cause distension of the joint capsule, affecting mechanoreceptors in the joint, and this effect may be more obvious in the OA knee which has presumably pre-existing arthritic damage to articular mechanoreceptors resulting from inflammation. It may evoke abnormal afferent discharge that decreases γ-motoneuron excitability, which would decrease muscle spindle sensitivity, and consequently decrease proprioceptive acuity[29,33,34]. In addition, increased IAP of the knee joint could result from the low compliance of the joint capsule[15], which in turn would cause a decline in proprioceptive acuity, thereby exaggerating the mechanical effects.

Another possible explanation for the proprioceptive deficit after joint infusion is arthrogenic reflex inhibition, *i.e.*, the selective quadriceps dysfunction and weakness found in subjects with knee OA or other knee diseases[35–37]. A few studies have identified quadriceps weakness after intra-articular knee joint effusion in healthy subjects[38–41]. In the present study, when the subjects actively reproduced the target angle in the NWB test, they extended their legs using concentric contraction of quadriceps muscle exclusively. If quadriceps muscle inhibition was generated after joint infusion, the knee JPS could be impaired under NWB conditions due to a poor neuromuscular control of knee extension. However, we did not evaluate quadriceps strength, and therefore further studies of the effects of joint effusion on arthrogenic muscle inhibition in OA knee joints are needed.

On the other hand, the proprioceptive decline after joint infusion was not significant in the WB test, despite the increasing tendency toward angular error in repositioning. As co-contractions of lower limb muscles and ipsilateral hip and ankle joint strategies could be used for repositioning the limb in the WB test, co-contractions of lower limb muscles and additional sensory input from adjacent hip and ankle joints may compensate for the proprioceptive decline in the knee joint. This possibility was supported by the recent observation of soleus motoneuron facilitation after joint effusion in healthy knee joints[42]. The proprioceptive deficit may also have been ameliorated by the use of bilateral hand supports, which were necessary to prevent participants' falling. Additionally, fluid redistribution in the joint could be expected during the NWB test after joint infusion. In support of this suggestion, McNair *et al.*[43] presented evidence of fluid shifting after exercise by volume calculation at different levels of the knee joint using MRI. Following repetitive knee flexion and extension movement during the NWB test, the fluid may be dispersed to other regions in the joint, thereby decreasing the overall strain in any one region and decreasing the mechanoreceptor discharge[43,44]. In addition, the number of subjects included was small, and therefore the risk of type II errors must be considered.

Some caveats regarding this study should be mentioned. First, the volume injected into the joint should be small to lessen the distinct effects of joint effusion. However, we felt that 20 mL would be adequate for joint distension in Korean subjects, as the mean height of our experimental subjects was 156.1 cm compared with 184.2 and 181.2 cm in other studies[38,39]. In addition, our infusion volume was clinically relevant, as the mean ± standard deviation (SD) volume of synovial fluid obtained by closed and open knee aspiration in advanced OA patients was reported previously to be 27.5 ± 15.5 mL[12]. Another study[45], in which 20 mL of intra-articular physiological saline and 2 mL of sodium hyaluronate for painful

Table II
AAEs (degrees) in the control and experimental groups*

	Control group ($n=20$)		Experimental group ($n=19$)		Adjusted mean difference†	
	Test 1	Test 2	Test 1	Test 2	Between groups	P-value
NWB test	5.19 (4.33–6.05)	4.74 (3.73–5.75)	4.84 (3.94–5.75)	5.95 (4.66–7.23)	1.41 (0.18–2.63)	0.025
WB test	2.73 (2.06–3.40)	2.86 (2.09–3.63)	3.07 (2.37–3.78)	3.75 (3.12–4.37)	0.47 (−0.28–1.23)	0.210

* Values are the means (95% CI).
† Differences between control and experimental groups are adjusted for age, BMI, K–L grade, and baseline scores as covariates.

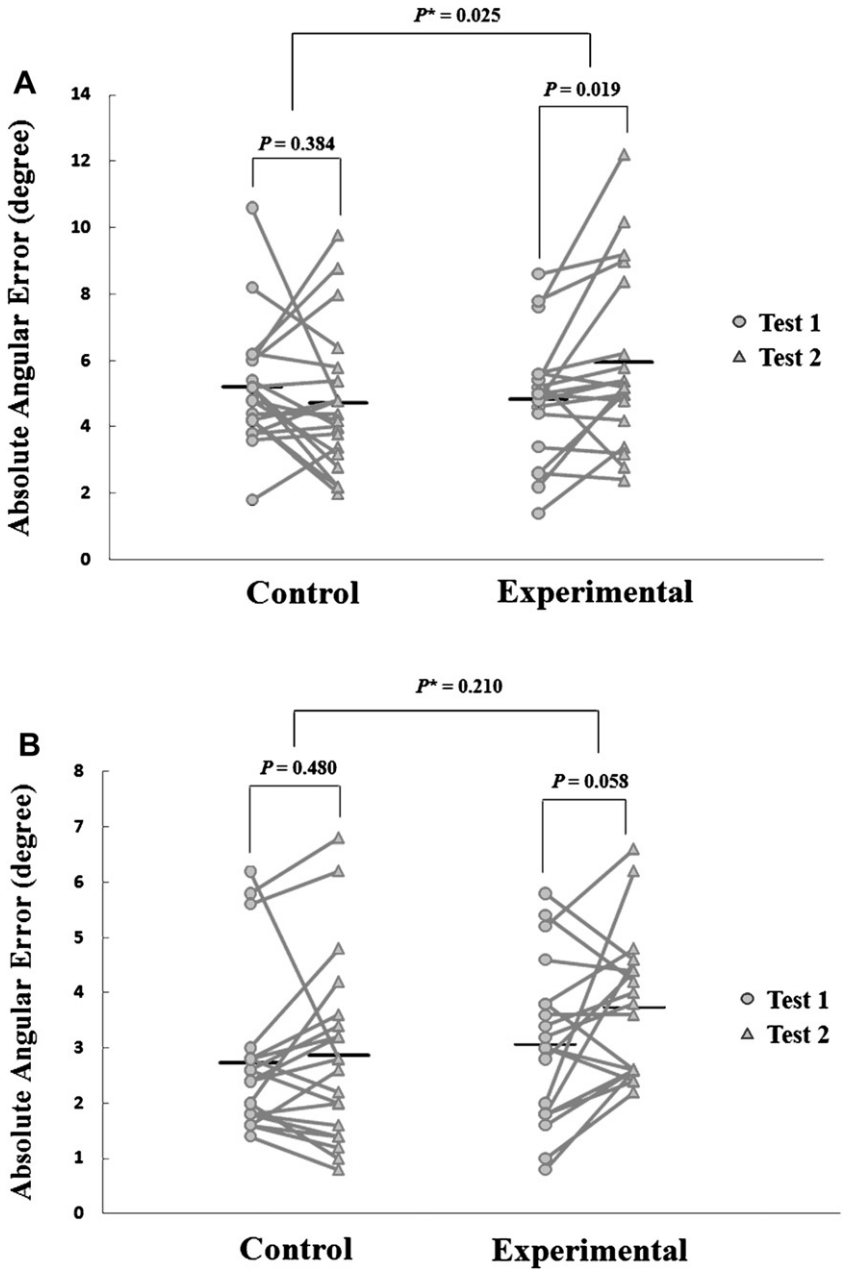

Fig. 2. AAEs in the control and experimental groups for NWB test (A). and WB test (B). Circles and triangles represent Test 1 and Test 2 values for individual subjects, respectively. Bars indicate the means of each trial. * Analyses are adjusted for age, BMI, K–L grade, and baseline scores as covariates.

knee OA did not show significant differences in reducing knee pain without adverse events, supported our use of 20 mL as the optimal injection volume for joint distension in patients with painful OA without any ethical problem. We also confirmed the fluid in the joint of all experimental subjects by US, and most reported a feeling of tightness or fullness in the joint during the injection procedure.

Second, pain associated with the injection may have influenced proprioception. However, some studies have shown that the knee effusion model allowed for mechanical effects of joint injury without the effects of perceived pain by demonstrating neuromuscular changes associated with joint effusion in the absence of pain[42,46]. In the present study, none of the experimental subjects complained of pain or discomfort during the measurement tasks. In addition, a previous study showed that proprioception did not improve after pain reduction in subjects with knee OA[47]. Therefore, the JPS changes after joint effusion would not be from pain, but from the effusion produced by the injection.

Third, we should consider the clinical relevance of our results. In a procedural perspective, we calculated ICCs to determine the test-retest reliability of the tests. The lower bound of the ICCs was somewhat low, indicating that more trials of testing JPS would produce more reproducible results. Although statistical significance was reached in our study, the relevance of a 1–2 degree difference also seems to have questionable significance in practical conditions. Further studies might be needed to evaluate the clinical impact of such a JPS decline on functional status in knee OA patients.

In conclusion, this study showed that the presence of fluid in the OA knee joint impairs the JPS, even though the injection material is not physiological inflammatory fluid. This suggests that joint effusion may be one of the various factors that contribute proprioceptive deficits in knee OA patients.

Author contributions

All authors made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Conflict of interest

The authors have declared no conflicts of interest.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.joca.2010.10.013.

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